

CLAIMS

1. A method for the identification of hetero-associating (poly)peptides comprising the steps of:

- (a) providing a library A of (poly)peptides/proteins comprising (poly)peptides A_m having the general formula:



wherein X represents a mixture of E, K, Q, and R, and wherein Z represents a mixture of N and V

- (b) providing a library B of (poly)peptides/proteins comprising (poly)peptides B_n having the general formula:



wherein X represents a mixture of E, K, Q, and R, and wherein Z represents a mixture of N and V;

- (c) combining in a common medium the (poly)peptides/proteins of said libraries A and B; and
- (d) screening or selecting for a screenable or selectable property caused by the hetero-association of a (poly)peptide A_m with a (poly)peptide B_n .

2. The method of claim 1 wherein said libraries A and B are provided by providing libraries of nucleic acid sequences encoding said (poly)peptides/proteins followed by causing or allowing the expression of said libraries of (poly)peptides/proteins.

3. The method of claim 2 wherein said common medium are host cells, each cell harbouring nucleic acid sequences encoding a (poly)peptide/protein of each of said libraries A and B.
4. The method of claim 3 wherein said (poly)peptides/proteins of said libraries A and B further comprise either a N- or a C-terminal fragment of the murine DHFR enzyme, and wherein said screenable or selectable property is insensitivity of the host cell to trimethoprim by reconstitution of the DHFR enzyme on hetero-association of (poly)peptides A_m and B_n .
5. A hetero-associating (poly)peptide A_m taken from the list of:
 - (a) WinZipA1: VAQLEE:KVKTLRAQNYELKSRVQRLREQVAQL
 - (b) WinZipA2: VAQLRE:RVKTLRAQNYELESEVQRLREQVAQL
 - (c) WinZipA3: VAQLQE:KVKTLRARNYELKSEVQRLLEEKVAQL
 - (d) WinZipA4: VAQLEE:QVKTLQARINYLKSKVQRLKEKVAQL
 - (e) WinZipA5: VAQLEE:RVKTLRAQNYELKSKVQRLLEEQVAQL
 - (f) WinZipA6: VAQLEE:QVKTLEAENYLKSKVQRLRERVAQL
 - (g) WinZipA7: VAQLQE:QVKTLEAQNYELESEVQRLKEQVAQL
 - (h) WinZipA8: VAQLEE:RVKTLKAENYELESEVQRLKERVAQL
 - (i) WinZipA9: VAQLEE:KVKTLKAKNYELKSKVQRLKEKVAQL
 - (j) WinZipA10: VAQLQEEVKT:QAENYELRSEVQRLLEEEVAQL
 - (k) WinZipA11: VAQLRERVKTLRAFNYELQSKVQRLKERVAQL
6. A hetero-associating (poly)peptide E_n taken from the list of:
 - (a) WinZipB1: VDELQAEVDQLQDENYALKTKVAQLRKKVEKL
 - (b) WinZipB2: VDELKA:EVDQLQDQNYALRTKVAQLRKEVEKL
 - (c) WinZipB3: VDELEA:EVDQLKDQNYALKTKVAQLQKQVEKL
 - (d) WinZipB4: VDELRA:KVDQLQDENYALETEVAQLQKRVEKL
 - (e) WinZipB5: VDELEA:EVDQLEDDQNYALQTRVAQLEKRVEKL
 - (f) WinZipB6: VDELKA:KVDQLKDQNYALRTKVAQLRKKVEKL

- (g) WinZipB7: VDELRAQIVDQIQDKNYALRTRVAQLKKRVEKL
- (h) WinZipB8: VDELQAEVDQIQDCNYALRTQVAQLKKKVEKL
- (i) WinZipB9: VDELRAQIVDQIQEDGNYALETQVAQLEKEVEKL
- (j) WinZipB10: VDELQAKVDQIQKDIENYALQTKVAQLQKRVEKL
- (k) WinZipB11: VDELFAEVDQIQLEDIENYALRTRVAQLRKQVEKL

7. A method for the identification of optimized hetero-associating (poly)peptides by using a hetero-associating (poly)peptide of claims 5 or 6 in a method according to anyone of claims 1 to 4, wherein a hetero-associating peptide WinZipA_m of claim 5 is used instead of library A of (poly)peptides/proteins comprising (poly)peptides A_m in step (a) of claim 1, or wherein a hetero-associating peptide WinZipB_n of claim 6 is used instead of library B of (poly)peptides/proteins comprising (poly)peptides B_n in step (b) of claim 1.
8. An optimized hetero-associating (poly)peptide obtainable by the method of claim 7.
9. A pair of hetero-associating (poly)peptides taken from the list of:
 - (a) WinZipA1 and WinZipB1
 - (b) WinZipA2 and WinZipB1
 - (c) WinZipA1 and WinZipB2
 - (d) WinZipA3 and WinZipB3
 - (e) WinZipA4 and WinZipB4
 - (f) WinZipA5 and WinZipB5
 - (g) WinZipA6 and WinZipB6
 - (h) WinZipA7 and WinZipB7

- (i) WinZipA8 and WinZip B8
- (j) WinZipA9 and WinZip B9
- (k) WinZipA10 and WinZip B10
- (l) WinZipA11 and WinZip B11

10. A (poly)peptide/protein comprising one of the hetero-associating (poly)peptides of claims 5 or 6, or an optimized hetero-associating (poly)peptide of claim 8, and a further (poly)peptide/protein.

11. A (poly)peptide/protein of claim 10 wherein said further (poly)peptide/protein is an enzyme, a toxin, a cytokine, a metal binding domain, a transcription factor, a member of the immunoglobulin superfamily, a bioactive peptide of 5 to 15 amino acid residues, a peptide hormone, a growth factor, a lectin, a lipoprotein, a peptide which is able to bind to an independent binding entity, or a functional fragment of any said further (poly)peptide/protein.

12. A hetero-associated (poly)peptide/protein comprising at least two (poly)peptide/proteins of claims 10 or 11, associated by hetero-association of a hetero-associating (poly)peptide A_m and a hetero-associating (poly)peptide B_n .

13. A DNA sequence encoding a hetero-associating (poly)peptide of claims 5 or 6, an optimized hetero-associating (poly)peptide of claim 8, or a (poly)peptide/protein of claims 10 or 11.

14. A DNA sequence encoding a hetero-associating (poly)peptide wherein said DNA sequence hybridizes under stringent conditions to a DNA sequence encoding a hetero-associating (poly)peptide of claims 5 or 6.

15. A vector comprising a DNA sequence of claim 13 or 14.
16. A vector comprising DNA sequences encoding at least two (poly)peptide/proteins of claims 10 or 11, comprising at least a hetero-associating (poly)peptide A_m and a hetero-associating (poly)peptide B_n .
17. A host cell containing at least one vector of claims 15 or 16.
18. A host cell of claim 17 which is a mammalian, preferably human cell, a yeast cell, an insect cell, a plant cell, or a bacterial, preferably E.coli cell.
19. A method for the production of a hetero-associating (poly)peptide of claims 5 or 6, an optimized hetero-associating (poly)peptide of claim 8, a (poly)peptide/protein of claims 9 or 10, or a hetero-associated (poly)peptide/protein of claim 12, which comprises culturing the host cell of claims 17 or 18 in a suitable medium, and recovering said (poly)peptide or said (poly)peptide/protein produced by said host cell.
20. A pharmaceutical composition comprising the hetero-associated (poly)peptide/protein of claim 12.
21. A diagnostic composition comprising the hetero-associated (poly)peptide/protein of claim 12.
22. A kit containing at least one of
 - (a) a hetero-associating (poly)peptide of claims 5 or 6, an optimized hetero-associating (poly)peptide of claim 8, or a (poly)peptide/protein of claims 10 or 11, or a hetero-associated (poly)peptide/protein of claim 12; or
 - (b) a vector of claims 16 or 17.